Experiment Number: S0594
Route: Dosed Feed, IV
Species/Strain: Rat/F344

Toxicokinetics Data Summary
Test Compound: Phenolphthalein
CAS Number: 77-09-8

Date Report Requested: 12/02/2016
Time Report Requested: 10:45:29
Lab: Research Triangle Institute

Male

	Treatment Groups (ppm)								
	375 [a, *]	**375 [b, #]**	**750 [c, *]**	**750 [d, #]**	**3000 [e, *]**	**3000 [f, #]**	**12000 [g, *]**	**12000 [h, #]**	**50000 [i, *]**
	Plasma								
C_{max} (ug/mL)	0.0958 ± 0.12	31.4 ± 12.0	1.05 ± 1.4	39.8 ± 3.4	0.173	108.0 ± 6.1	0.295 ± 0.37	261.0 ± 32.0	0.201 ± 0.044
AUC_{0-t} (ug*hr/mL)	0.937 ± 0.15	540.0 ± 32.0	6.57 ± 1.7	753.0 ± 21.0	2.69 ± 0.17	2115.0 ± 40.0	3.12 ± 0.51	4752.0 ± 130.0	2.80 ± 0.20

Experiment Number: S0594
Route: Dosed Feed, IV
Species/Strain: Rat/F344

Toxicokinetics Data Summary
Test Compound: Phenolphthalein
CAS Number: 77-09-8

Date Report Requested: 12/02/2016
Time Report Requested: 10:45:29
Lab: Research Triangle Institute

Male

	Treatment Groups (ppm)		
	50000 [j, #]	**25 IV [k, *]**	**25 IV [l, #]**
	Plasma		
C_{max} (ug/mL)	226.0 ± 50.0	210.0 ± 13.0	22.4 ± 1.3
AUC_{0-t} (ug*hr/mL)	4494.0 ± 128.0	56.0 ± 0.35	290.0 ± 34.0

Experiment Number: S0594
Route: Dosed Feed, IV
Species/Strain: Rat/F344

Toxicokinetics Data Summary
Test Compound: Phenolphthalein
CAS Number: 77-09-8

Date Report Requested: 12/02/2016
Time Report Requested: 10:45:29
Lab: Research Triangle Institute

Female

	Treatment Groups (ppm)								
	375 [m, *]	**375 [n, #]**	**750 [o, *]**	**750 [p, #]**	**3000 [q, *]**	**3000 [r, #]**	**12000 [s, *]**	**12000 [t, #]**	**50000 [u, *]**
	Plasma								
C_{max} (ug/mL)	0.169	30.2 ± 12.0	0.938 ± 1.5	61.1 ± 15.0	0.454 ± 0.56	145.0 ± 12.0	0.762	271.0 ± 49.0	1.85 ± 3.1
AUC_{0-t} (ug*hr/mL)	0.566 ± 0.00	508.0 ± 18.0	4.23 ± 1.8	984.0 ± 29.0	2.10 ± 0.65	2747.0 ± 53.0	3.77 ± 1.5	4940.0 ± 92.0	6.13 ± 3.6

Experiment Number: S0594
Route: Dosed Feed, IV
Species/Strain: Rat/F344

Toxicokinetics Data Summary
Test Compound: Phenolphthalein
CAS Number: 77-09-8

Date Report Requested: 12/02/2016
Time Report Requested: 10:45:29
Lab: Research Triangle Institute

Female

	Treatment Groups (ppm)		
	50000 [v, #]	**25 IV [k, *]**	**25 IV [l, #]**
	Plasma		
C_{max} (ug/mL)	231.0 ± 14.0	166.0	40.4 ± 34.0
AUC_{0-t} (ug*hr/mL)	4352.0 ± 117.0	43.0 ± 0.69	383.0 ± 22.0

LEGEND

Data are displayed as mean ± SD

MODELING METHOD & BEST FIT MODEL

[a] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 24.86 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[b] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 24.86 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[c] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 48.76 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[d] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 48.76 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[e] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 176.24 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[f] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 176.24 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[g] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 606.24 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[h] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 606.24 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[i] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2783.39 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

LEGEND

MODELING METHOD & BEST FIT MODEL

[j] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2783.39 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[k] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule.; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[l] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[m] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 25.61 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[n] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 25.61 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[o] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 51.58 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[p] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 51.58 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[q] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15 Mean daily dose is 180.50 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[r] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15 Mean daily dose is 180.50 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[s] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 714.28 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

LEGEND

MODELING METHOD & BEST FIT MODEL

[t] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 714.28 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

[u] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2927.10 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

[v] Excel, Version 7 used to calculate means and standard deviation for Cmax, Cmax steady state and AUC24-hr by trapezoidal rule. To determine AUC24-hr, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2927.10 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

ANALYTE

[#] Phenolphthalein Glucuronide

* Phenolphthalein

TK PARAMETERS

C_{max} = Observed or Predicted Maximum plasma (or tissue) concentration

AUC_{0-t} = Area under the plasma concentration versus time curve, AUC, from time t_i (initial) to t_f (final), AUC_{last}

** END OF REPORT **